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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/617,910	07/10/2003	Gillian Daphne Elliott	5759-66308-01	4218

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KLARQUIST SPARKMAN CAMPBELL
LEIGH & WHINSTON, LLP
One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, OR 97204-2988

EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/617,910	ELLIOTT, GILLIAN DAPHNE	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-18* is/are pending in the application.

4a) Of the above claim(s) *13-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12, 17, 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37.CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 12-18 are pending in the application.

2. In the prior action, mailed on February 23, 2005, claims 12-16 were pending, with claim 12 rejected, and claims 13-16 withdrawn as to non-elected inventions. In the Response of August 22, 2005, the Applicant amended claim 12, and added new claims 17 and 18.

Claims 12, 17, and 18 are presently under consideration.

Specification

(Prior Objection- Withdrawn) The disclosure was objected to because of the following informalities: the term "concnern" on line 9 of page 9 appears as though it should read - - concern- -. In view of the amendment to the specification, the objection is withdrawn.

Claim Objections

3. **(Prior Objection- Withdrawn)** Claim 12 was objected to as lacking a comma between the phrases "a covalent coupling" and "and a non-covalent association" in line 3 of the claim. In view of the amendment of the claim, the objection is withdrawn.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. **(Prior Rejection- Withdrawn)** Claim 12 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite as it was unclear what was meant by the phrase "a microtubule binding function of VP22." In view of the amendment of the claim such that it now merely requires that the protein binds microtubules, the rejection is withdrawn.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. **(Prior Rejection- Maintained)** Claim 12 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim was rejected on two grounds. First, the claim was rejected as reading on the use of any herpesviral VP22 protein, where the application only discloses the use of the HSV1 VP22 protein. In view of the amendment of the claim limiting it to the use of the HSV1 VP22 protein, this portion of the rejection is withdrawn.

Second, the claim was rejected because the application lacks sufficient written description support for any portion or derivative of the HSV1 VP22 that binds to microtubules. For the reasons indicated below, this portion of the rejection is maintained, and extended to new claims 17 and 18.

The Applicant has cancelled the reference to derivatives to the HSV1 VP22 protein, but traverses the rejection with respect to the portions of the protein. The traversal is on the basis of teachings in the application with respect to certain fragments of the protein shown to be capable

of binding microtubules. In particular, the application demonstrates that fragments comprising residues 1-267, 1-191 of the 301 amino acid protein were capable of binding to microtubules, and that a fragment comprising residues 1-172 of the protein had an attenuated microtubule binding activity. It is therefore accepted that there is support for these embodiments.

Further, the Applicant also notes that the application teaches the deletion of residues 160-173 "has substantially reduced ability to bind to microtubules." Response, page 7. From this, the Applicant concludes that there is a correlation between these residues and the function of microtubule binding. However, while the Examiner agrees with the Applicant that these residues do appear to be involved in microtubule binding, the application has not demonstrated that these residues are sufficient for microtubule binding. The reference teaches that there is substantial reduction in the ability of the protein to bind to the microtubules, not that the ability is lost altogether. Thus, it appears that there are other residues involved in the interaction. Further, while the application states that a removal of this region lead to a reduced ability to bind microtubules, there is no evidence that the indicated region is itself capable of microtubule binding. There is therefore insufficient disclosure of the minimum required residues or structure from the VP22 protein that would enable a conjugate comprising such to bind microtubules. Thus, while the Applicant may have provided examples falling within the claimed genus, these examples are not sufficient to demonstrate possession of every portions of the HSV1 VP22 protein that binds to microtubules because there is no disclosure of the minimum binding domain required for this function.

The rejection is therefore maintained for the reasons above and the reasons of record. Further, the rejection is extended to new claims 17 and 18.

8. **(New Rejection- Necessitated by Amendment)** Claims 12 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claim 12 reads on methods of delivering a substance to microtubules, and has been amended to read on embodiments wherein the substance is a microtubule-binding drug. Newly added claim 18 identifies the drug as colchicine. Because the claims are drawn to methods for the delivery of a drug, the claims are read as requiring some therapeutic effect. These claims are rejected as the application does not provide adequate teachings to enable those in the art to use the claimed methods. In particular, the teachings of the application raise questions as to the therapeutic effect of a conjugation of VP22 and a microtubule-binding drug such as colchicine.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 ¶ 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988); and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered. In the present case, the factors considered most relevant are

the presence or absence of working examples, the direction and guidance presented, and the breadth of the claims.

As indicated above, the claims are drawn to methods of using a conjugate of VP22 with a microtubule-binding drug. In particular, the claims have indicated colchicine as an example of a drug that may be delivered according to the claimed method. Colchicine is described in the art as a drug that causes the depolymerization of microtubules. See e.g., U.S. 5,583,153, column 4, lines 17-18. Based on these teachings, those in the art would read the claimed method of claim 1 as including embodiments for the delivery of drugs that cause microtubule depolymerization. However, while the application suggests the use of VP22 for the delivery of colchicine, it does not provide any demonstration of the effects that such a delivery method would achieve. While this would not be material if VP22 merely bound to the microtubules, this is not the sole activity attributed to the protein.

In addition to the microtubule binding function of the protein, the application also teaches on pages 13-14 (and in Figure 2) that VP22 has the effect of stabilizing microtubules against the effects of microtubule binding agents. In particular, the application demonstrates that VP22 "can stabilize MTs against depolymerising agents." Page 14, line 7. Thus, the application teaches that VP22 has a counter activity to drugs, such as colchicine, leading to the depolymerization of microtubules. From these teachings it is not clear what the effect of combining a depolymerizing drug such a colchicine with a stabilizing molecule such as VP22 would have on the cell to which the conjugate is delivered. In view of the teachings of the reverse effects of these two components, and the lack of any demonstration as to what the effect of the combination would be, the application is not enabling for methods of using VP22 for the delivery of colchicine or

related drugs. This is because, as those in the art would not know what the therapeutic effect, if any, of the combination of VP22 with a drug such as colchicine would be, they have not been enabled for the use of the combination.

Claim Rejections - 35 USC § 102

9. **(Prior Rejection- Withdrawn)** Claim 12 was rejected under 35 U.S.C. 102(b) as being anticipated by either of WO 97/05265 or Elliott et al. (Cell 83:223-233). In view of the amendment of the claims limiting them to the transport of drugs that bind to microtubules, the rejection is withdrawn.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. **(Prior Rejection- Withdrawn)** Claim 12 was rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-8 of U.S. Patent No. 6184038. In view of the amendment of the claim such that it now reads on the delivery of microtubule binding drugs, the rejection is withdrawn.

12. **(Prior Rejection- Withdrawn)** Claim 12 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16 of U.S. Patent No. 6017735. In view of the amendment of the claim such that it now reads on the delivery of microtubule binding drugs, the rejection is withdrawn.

13. **(Prior Rejection- Withdrawn)** Claim 12 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 10 of U.S. Patent No. 6251398. In view of the amendment of the claim such that it now reads on the delivery of microtubule binding drugs, the rejection is withdrawn.

Conclusion

14. No claims are allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 9/19/05

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600